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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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EXAMINER

SHAHNAN-SHAH, KHATOL S

ART UNIT PAPER NUMBER

1645

DATE MAILED: 12/19/2001

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/616,247

Applicant(s)

CARSON ET AL.

Examiner

Khatol S Shahnan-Shah

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 September 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10,12 and 18-31 is/are pending in the application.
- 4a) Of the above claim(s) 12 and 25-31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10 and 18-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 10,12 and 18-31 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

1. The Examiner of U.S. Patent application SN 09/616,247 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Examiner Shahnan-Shah, Technology Center 1600, Art Unit 1645.

2. Currently claims 10, 12 and 18-31 are pending.

Election/Restrictions

3. Applicants' response to restriction requirement of September 4, 2001, paper No. 5 is acknowledged.

Applicants elected group I, claims 10 and 18-24 with traverse, which is drawn to a vaccine (gene therapy vaccine). No arguments were set forth by the applicants.

Claims 12 and 25-31, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected group II.

4. Applicants' preliminary amendment of September 4, 2001, paper No. 6 is acknowledged.

Claims 10 and 18-24 were amended.

5. Claims 10 and 18-24 are under consideration.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 10 and 18-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a DNA composition useful in inducing immune protection against arthritogenic peptides in a host comprising a recombinant gene expression vector which encodes bacterial dnaJp1 peptide. The specification is not enabled for a DNA composition useful in inducing immune protection against arthritogenic peptides in a host comprising a recombinant gene expression vector, which encodes bacterial dnaJp1 peptide.

The specification discloses various in vitro experiments that demonstrate antibody binding to rdnaJ, inhibition studies and binding of rdnaJ to lymphocytes from patients with RA, however the specification does not teach a skilled artisan how to administer the claimed composition for immune protection. The specification presents a paper protocol in this regard. The specification has not taught a skilled artisan how to use the invention as presently claimed. Applicants have not shown or disclosed a correlation between in vitro and in vivo studies or that there are animal models that correlate to human (i.e. person) efficacy.

The specification fails to provide an enabling disclosure for the preparation and use of a DNA composition, including expression vector compositions comprising nucleic acids encoding antigens because it fails to provide adequate guidance regarding how one would have prepared a nucleic acid which when introduced into a host would induce an immune response against the protein encoded by said nucleic acid. In contrast to direct protein immunogens, nucleic acids are required to target appropriate cell types within a host, become transcriptionally active, appropriately process any encoded proteins and present such proteins to the host in a manner suitable for recognition by the host's immune system. Such a "**gene therapy**" approach to epitope delivery suffers from all the limitations associated with gene therapy technology. However, as of 12/95, the artisan did not accept, in the absence of suitable and particular

guidance, that such could have been accomplished without having had to have exercised undue experimentation. See e.g. NIH Report Reference.

Applicants' specification fails to provide guidance to the skilled artisan on the parameters for DNA vaccine for the breadth of the claimed invention. Numerous factors complicate the gene therapy art, which have not been shown to be overcome by routine experimentation. These include, the fate of the DNA vector itself (volume of distribution, rate of clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced. These factors differ dramatically based on the vector used, the protein being produced, and the disease being treated.

Additionally, the specification does not provide any working examples which enable the claimed invention. Nor does the specification provide any guidance to the skilled artisan on how to make and use genetic constructs which would result in the desired effect. Even assuming that an effective genetic material is constructed, it is not evident that enough cells can be transfected to provide any therapeutic benefit.

Several recent reviews indicate that efficient delivery and expression of foreign DNA has not yet been achieved by any method. Marshall (*Science*, 269:1050-1055, August, 1995) states that "there has been no unambiguous evidence that genetic treatment has produced therapeutic

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benefits" (page 1050, column 1) and that "difficulties in getting genes transferred efficiently to target cells- and getting them expressed- remain a nagging problem for the entire field" (page 1054, column 3). James Wilson, one skilled in the art, is quoted in the Marshall article as saying that "[t]he actual vectors- how we're going to practice our trade- haven't been discovered yet" (page 1055, column 2). Miller et al (*FASEB J.*, 9:190-199, 1995) also review the types of vectors available for *in vivo* gene therapy, and conclude that "for the long-term success as well as the widespread applicability of human gene therapy, there will have to be advances...targeting strategies outlined in this review, which are currently only at the experimental level, will have to be translated into components of safe and highly efficient delivery systems" (page 198, column 1). Therefore, even if the specification enabled the construction of the gene delivery vehicle comprising a cell targeting element, in the absence of particular guidance, the artisan would have been required to develop *in vivo* and *ex vivo* means of practicing the claimed methods and such development in the nascent and unpredictable gene therapy art would have been considered to have necessitated undue experimentation on the part of the practitioner.

Furthermore the art teaches that EBV is possibly the cause of RA (col. 3, l. 4-14) and the administration of anti-inflammatory agents, not the virus itself (cols. 4-6) (Carson 5,310,732 and Carson et al. WO 90/14835). Hyman discloses that RA may be caused by a bacterial source, bacteria are associated with RA (col. 5), however they do not suggest or use bacterial polynucleotides in a vaccine preparation for administration to induce immune protection to treat RA in a person. Rather Hyman uses antibiotics effective against the bacteria and additional antibiotics such as kanamycin or neomycin for example (col. 27; claims). It is unclear from the art what is the etiological cause of RA, and therefore would be unclear and an undue burden to a

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skilled artisan to determine what type of composition to administer to a person with RA to reduce its exposure or predisposed to develop RA. Should antibiotics, anti-inflammatory agents, or EBV or some bacterial protein or nucleic acid be administered to stimulate an immune response or some combination of the above? In view of the reasons set forth, there would be undue experimentation for a skilled artisan to practice the claimed invention.

A disclosure in an application, to be complete, must contain such description and details as to enable any person skilled in the art or science to which it pertains to make and use the invention as of its filing date, *In re Glass*, 181 USPQ 31; 492 F.2d 1228 (CCPA 1974). While the prior art setting may be mentioned in general terms, the essential novelty, the essence of the invention, must be described in such details, including proportions and techniques where necessary, as to enable those persons skilled in the art to make and utilize the invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claims 10 and 18-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10, 18, 19, 20, 21 and 22 are vague and indefinite because they recite the abbreviations (dnaJ) and (dnaJp1). Full terminology should be used, at least in the primary claim.

Claim 24 is vague and indefinite because it recites an abbreviation (TGF- β). Full terminology should be used, at least when an abbreviation appears in the claim for the first time.

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Claim 20 is a duplicate of claim 18.

Claim 21 is a duplicate of claim 19.

8. No claims are allowed.

9. The references cited or used as prior art in support of one or more rejections in the instant office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record in the parent application Serial No. 08/618464.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached on 7:30 AM - 4 PM from Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah 12/15/01

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

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[Signature]
NITA MINNIFIELD
PRIMARY EXAMINER
12/17/01